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10,177,141 03/27/95 APR 1

EXAMINER

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ART UNIT PAPER NUMBER

1912

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DATE MAILED: 03/29/97

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on \_\_\_\_\_ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.  
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

- |   |  |
|---|--|
| 1. <input checked="" type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input checked="" type="checkbox"/> Notice of Draftsman's Patent Drawing Review, PTO-948. |
| 3. <input checked="" type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449.      | 4. <input type="checkbox"/> Notice of Informal Patent Application, PTO-152.                  |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474.     | 6. <input type="checkbox"/> _____  |

**Part II SUMMARY OF ACTION**

1. ☒ Claims 1-18 are pending in the application.  
Of the above, claims \_\_\_\_\_ are withdrawn from consideration.
2. ☐ Claims \_\_\_\_\_ have been cancelled.
3. ☐ Claims \_\_\_\_\_ are allowed.
4. ☒ Claims 1-18 are rejected.
5. ☐ Claims \_\_\_\_\_ are objected to.
6. ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on \_\_\_\_\_. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed \_\_\_\_\_, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

**EXAMINER'S ACTION**

**BEST AVAILABLE COPY**

### ***Double Patenting***

1. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and <sup>©</sup> may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 8-9, and 15-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-9, 14-17, and 22-24 of copending Application No. 08/398,852. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth below.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-2 and 8-9 of the present application encompass administration of IGF-I, IGF-II, or a combination of IGF-I and IGF-II to effect a change in the central nervous system or treat a disorder or disease in the brain, while claims 15-16 of the present application encompass administration of a combination of IGF-I and IGF-II to effect a change in the spinal cord or treat a disorder or trauma in the spinal cord. The claims 6-9, 14-17, and 22-24 of the copending Application No. 08/398,852 encompass administration of IGF-I, IGF-II, or a combination of IGF-I and IGF-II to treat diabetic neuropathy which includes the central nervous system(CNS). Since the terms "effect a change in CNS" or "treat a disorder or disease in the brain" of the claims 1-2 and 8-9 in the present application encompass treating the diabetic neuropathy in CNS, it satisfies the limitations of claims 6-9, 14-17, and 22-24 of the copending Application No. 08/398,852. The terms "effect a change in the spinal cord" or "treat a disorder or disease in the spinal cord" of the claims 15-16 in the present application encompass treating the diabetic neuropathy including the CNS because spinal cord is part of the CNS, and thus it satisfies the limitations of claims 6-9, 14-17, and 22-24 of the copending Application No. 08/571,802. Thus it

would be prima facie obvious to administer IGF-I, IGF-II, or a combination of IGF-I and IGF-II to treat the whole genus of diabetic neuropathy including the central nervous system(CNS) using the teachings of the copending Application No. 08/571,802.

***Claim Rejections - 35 USC § 112***

2. Claims 1-4, 7-11, and 14-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of parenteral administration of IGF-I, IGF-II, or a combination of both IGF-I and II for the treatment of locus ceruleus noradrenergic neurons ablation by 6-hydroxydopamine, does not reasonably provide the full scope of enablement for parenteral administration of IGF-I or IGF-II, for effecting any changes in the central nervous system (CNS) or spinal cord and treating any disorders or diseases in the brain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 3-4, 8, and 10-11 encompass effecting all changes in the CNS which includes molecular, physiological, cellular, and

behavioral changes by administering IGF-I or IGF-II under normal or disordered conditions. Claim 15 and 17-18 encompass effecting all changes in the spinal cord which includes molecular, physiological, cellular, and behavioral changes by administering IGF-I or IGF-II under normal or disordered conditions. Claims 1-4, 8-11, and 15-18 encompass treating a disorder or a disease in the brain or a disorder or trauma to the spinal cord by administering IGF-I or IGF-II. Claims 7 and 14 are directed to AIDS dementia. However, the specification fails to teach effecting any changes in the CNS or the spinal cord by administering IGF-I or IGF-II nor treating a disorder or trauma to the spinal cord or disorder or a disease in the brain including AIDS dementia. Effecting any changes in the CNS or spinal cord includes functions in the CNS from molecular, cellular, physiological, neural network, to behavior in normal and disordered state and the state of the art at the time of the invention provides no reference to indicate that administering IGF-I or -II will affect any changes in the CNS or spinal cord. Just a few examples of effecting a change in CNS are changes to schizophrenia, depression, spinal cord transection, ion channel modulation, or memory which the state of the art is silent with

respect to treatment with IGF-I or II. Baringa (A34) provides the state of the art after the time of the invention where treatments of nervous system diseases with neurotrophic factors are unpredictable and that treatment of any one disease is not predictive of another. Baringa further indicates that although treating peripheral neuropathy may be more promising, even with sensory peripheral neuropathy, there is a difference between diabetic neuropathy and cancer chemotherapy induced neuropathy (A34, page 774, left column). Thus, the treatment of a nervous system disease is an unpredictable art where one model of treatment for neuropathy is not predictive of the another model of treatment. Although the specification provides working examples of IGF-II mRNA changes in the streptozotocin induced diabetic rat brain by administration of IGF-I (pages 11-12) and working examples of IGF-II administration for treatment of 6-hydroxydopamine (6OHDA) induced noradrenergic locus ceruleus ablation by measuring limb withdrawal reflex, such examples are not predictive of effecting any changes in CNS or spinal cord, or treating any disorders or diseases in the brain or spinal cord, because the state of the art indicates that any one model of treatment for a disease is not predictive of the another model of

treatment. Further indication that treatment of neurological disease is an unpredictable art is indicated by Jackowski(R) who teaches that neurons do not regenerate the CNS because CNS environment is non-supportive or actively inhibitory to neuronal regeneration (reference R is cited as being of interest to applicant's specification, page 305, right column, bottom paragraph). Working example in the specification of IGF-II administration for treatment of 6-hydroxydopamine (6OHDA) induced noradrenergic locus ceruleus ablation by measuring limb withdrawal reflex is not predictive of treating any disorders or diseases in the brain or spinal cord, because the state of the art indicates that CNS is inhibitory to neuronal regeneration and regeneration is necessary for treatment of CNS diseases. Shepherd(S) disclose the state of the art by teaching how the CNS is categorized and the noradrenergic neurons of the locus ceruleus is but a small region in the whole CNS and the noradrenergic neurons of the locus ceruleus are different from other regions of the brain such as the dopaminergic neurons of the striatum(reference S is cited as being of interest to applicant's specification, page 499, figure 24.9 and section "Norepinephrine"; page 501, figure 24.10 and left column). Since

the treatment of CNS is an unpredictable art because the CNS is inhibitory to regeneration, the working example for treatment of noradrenergic locus ceruleus is not predictive of any other regions of the brain nor any other types of neurons. Finally, the treatment of AIDS dementia is an unpredictable art and the state of the art at the time of the invention does not indicate any reference that administering IGF-I or -II will be effective in treatment of AIDS dementia. Barnes(T) teaches the state of the art at the time of the invention regarding how AIDS virus injures the nervous system and indicates uncertainty and controversy about the mechanism of the injury (S, page 1574, left column, top paragraph). Barne's discussion concerning AIDS dementia is limited to the etiology and no discussion concerning treatment with IGF-I or II is provided (S, page 1574, left column, top paragraph). The working examples are not predictive of treating AIDS dementia because the specification fails to provide a model for AIDS dementia which could be used predict the effect of treatment by administering IGF-I or -II. Without such guidance, the determination of IGF-I or -II effect on treating AIDS dementia requires empirical experimentation and are not predictive of treating AIDS dementia. Thus without further



guidance, it would require undue experimentation to determine all the changes effected in the CNS or spinal cord by administering IGF- or IGF-II as well as all the disorders of the brain or spinal cord including AIDS dementia.

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371<sup>©</sup> of this title before the invention thereof by the applicant for patent.

4. Claims 1-6, 8-13, and 15-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Lewis et al. (A1).

Lewis et al. disclose the method of parenteral administration of IGF-I or IGF-II to enhance the survival of neuronal cells for treatment of Alzheimer's disease or Parkinson's disease (column 3, bottom paragraph; column 4, column, lines 18-29). Lewis et al. disclose the method of parenteral administration of IGF-I or IGF-II to enhance the

survival of neuronal cells where the neuronal cells are from the CNS (column 4, lines 41-50) or the brain or the spinal cord (column 9, lines 1-29). Lewis et al. disclose the different methods of measurements for enhancing the survival of neuronal cells (column 4, lines 41-68). Lewis et al. disclose the method of parenteral administration of IGF-I or IGF-II with specific dosage ranges of 1ug/kg/day to 1 g/kg/day as well as ranges 0.01 mg/kg/day to 100mg/kg/day (column 10, lines 3-22).

Claim limitations to "effecting a change" and "treating a disorder or a disease" is anticipated by the method of Lewis et al. discussed immediately above.

5. No claims are allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Pak whose telephone number is (703) 305-7038. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957. The fax phone number for this Group

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is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

*MPP*  
Michael D. Pak  
1812  
14 March 1997

*Stephen Walsh*  
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SUPERVISORY PATENT EXAMINER  
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